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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,514	04/30/2001	K. Roger Aoki	D2929CON	3428

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EXAMINER	
FORD, VANESSA L	
ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 12/20/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,514	AOKI ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 17-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 17-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

FINAL ACTION

1. This Office Action is responsive to Applicant's response in paper No. 5 to the first Office Action in paper No. 3.

2. The amendment submitted September 27, 2001 is acknowledged. Claims 27-29 have been added. Claims 1-9 and 17-29 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

4. In view of Applicant's amendment concerning formal matters the objections to the declaration are withdrawn.

5. In view of Applicant's amendment and Response, the rejections under 112, first and second paragraph are withdrawn.

6. The rejection of claims 17-26 and newly submitted claims 27-29 under 35 U.S.C. 102(b) as anticipated by Ciccarelli et al is being maintained for the reasons set forth in paper 3, page 7-8 of the previous Office Action.

The rejection was on the grounds that Ciccarelli et al teach the cultural and physiological characteristics of *Clostridium botulinum* type G and susceptibility of certain animals to its toxin (see title). Ciccarelli et al teach a composition for cross-neutralization tests comprising one volume of undiluted type G antitoxin mixed with 5 volumes of botulinal toxin types A, B, C, D, E, F and G containing 10 to 20 mouse LD_{50}/0.5 ml. The mixtures were incubated at 37°C for 30 minutes, after which 0.6 ml of

each was injected into each member of a separate mouse pair. Toxins A through F were standard toxins in 50% glycerol, which are used to determine antitoxin levels in various sera (p. 844, 2nd column). Characteristics such as therapeutically effective amount and selected to control duration would be inherent in the composition of the prior art.

Since the Office does not have the facilities for examining and comparing applicant's botulinum toxin composition with the botulinum toxin composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the botulinum toxin composition of the prior art does not possess the same material structural and functional characteristics of the claimed botulinum toxin composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that Ciccarelli et al does not disclose or suggest compositions comprising at least two neurotoxins selected from a group consisting of botulinum types A, B, C, D,E, F and G as recited in the claims. Applicant further urges that Ciccarelli et al does not disclose or suggest compositions comprising a combination of botulinum toxin types A and B or types A and E.

It is the Examiner's position that Ciccarelli et al teach a composition that comprises at least two neurotoxins selected from a group consisting of botulinum types A, B, C, D, E, F and G as recited in the claims. Ciccarelli et al teach a composition that comprises a mixture of undiluted type G antitoxin and botulinum types A, B, C, D, E, F and G which is a composition that comprises at least two types of botulinum. A mixture is define as a composition of two or more substances not chemically bound to each other *(Webster's II New Riverside University Dictionary, The Riverside Publishing Company, 1988)*. Therefore, the composition of Ciccarelli et al is a composition comprising at least two neurotoxins. It is well known in the art that compositions containing mixtures of neurotoxins are used for therapeutic purposes. This is evidenced

by Jankovic et al, (*The New England Journal of Medicine, April 25, 1991, p. 1186-1194)* that suggest that patients with antibodies against botulinum will respond to injections with other botulinum toxins that are immunogenically distinct from type A (page 1189, 1st column, second paragraph) and Pearce et al, *(U.S. patent No. 6,087,327, published July 11, 2000)* that suggest the use of admixtures of neurotoxins provide clinical benefits to patients by lengthening intervals between neurotoxin treatments, reducing adverse immunogenic responses to neurotoxins and reducing adverse diffusion-dependent side-effects of neurotoxin treatments (see the Abstract). It is the Examiner's position that the composition of Ciccarelli, et al appears to be the same as the claimed invention.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jankovic et al *(The New England Journal of Medicine, April 25, 1991)* in view of *Ciccarelli* et al *(Applied and Environmental Microbiology, Dec. 1977, p.843-848)*.

Claims 1-9 are drawn to a method of treating a patient suffering from a neuromuscular disorder or condition comprising administering to a patient ~~with~~ at least two neurotoxins selected from the group consisting of botulinum toxin types A, B, C, D, E, F and G.

Jankovic et al teaches methods of administering botulinum toxin A to patients in order to treat neuromuscular disorders and conditions such as Strabismus, Dystonias, Blepharospasm, Cervical Dystonia (Spasmodic Torticollis), Oromanibular Dystonia, Spasmodic Dysphonia (Laryngeal Dystonia) and other conditions (see the entire document).

Jankovic et al do not teach the use of botulinum types B, C ,D,E, F or G.

Ciccarelli et al teach a composition comprising one volume of undiluted type G antitoxin mixed with 5 volumes of botulinal toxin types A, B, C, D, E, F and G p. 844, 2nd column).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the botulinum composition as taught by Ciccarelli et al to the composition of botulinum A used in the method of treating neuromuscular disorders as taught by Jankovic because Jankovic et al teach that patients with antibodies against botulinum toxin A will respond to injections with other botulinum that are immunogenically distinct from type A (p. 1189, 1st column).

Pertinent Prior Art

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Greene et al, Movement Disorders, 1993, Volume 8, No. 4, p. 479-483).*

Status of Claims

9. No claims are allowed.

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
December 16, 2001

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